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### **The eHealth self-management application 'Oncokompas' that supports cancer survivors to improve health-related quality of life and reduce symptoms**

van der Hout, A.; Holtmaat, K.; Jansen, F.; Lissenberg-Witte, B.; Van Uden-Kraan, C. F.; Nieuwenhuijzen, G. A. P.; Hardillo, J. A.; de Jong, R. J. Baatenburg; Tiren-Verbeet, N. L.; Sommeijer, D. W.; de Heer, K.; Schaar, C. G.; Sedee, R. J. E.; Bosscha, K.; van den Brekel, M. W. M.; Petersen, F.; Westerman, M.; Honings, J.; Takes, R. P.; Houtenbos; van den Broek, W. T.; de Bree, R.; Jansen, P.; Eerenstein, S. E. J.; Leemans, C. R.; Zijlstra, J. M.; Cuijpersa, P.; Van De Poll-Franse, L. V.; Verdonck-de Leeuw, I. M.

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## The eHealth self-management application 'Oncokompas' that supports cancer survivors to improve health-related quality of life and reduce symptoms: which groups benefit most?

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









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## The eHealth self-management application ‘Oncokompas’ that supports cancer survivors to improve health-related quality of life and reduce symptoms: which groups benefit most?

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### ABSTRACT

**Background:** Oncokompas is a web-based self-management application that supports cancer survivors to monitor their health-related quality of life (HRQOL) and symptoms, and to obtain personalised feedback and tailored options for supportive care. In a large randomised controlled trial among survivors of head and neck cancer, colorectal cancer, and breast cancer and (non-)Hodgkin lymphoma, Oncokompas proved to improve HRQOL, and to reduce several tumour-specific symptoms. Effect sizes were however small, and no effect was observed on the primary outcome patient activation. Therefore, this study aims to explore which subgroups of cancer survivors may especially benefit from Oncokompas.

**Materials and methods:** Cancer survivors ( $n = 625$ ) were randomly assigned to the intervention group (access to Oncokompas,  $n = 320$ ) or control group (6 months waiting list,  $n = 305$ ). Outcome measures were HRQOL, tumour-specific symptoms, and patient activation. Potential moderators included socio-demographic (sex, age, marital status, education, employment), clinical (tumour type, stage, time since diagnosis, treatment modality, comorbidities), and personal factors (self-efficacy, personal control, health literacy, Internet use), and patient activation, mental adjustment to cancer, HRQOL, symptoms, and need for supportive care, measured at baseline. Linear mixed models were performed to investigate potential moderators.

**Results:** The intervention effect on HRQOL was the largest among cancer survivors with low to moderate self-efficacy, and among those with high personal control and those with high health literacy scores. Cancer survivors with higher baseline symptom scores benefitted more on head and neck (pain in the mouth, social eating, swallowing, coughing, trismus), and colorectal cancer (weight) specific symptoms.

**Discussion:** Oncokompas seems most effective in reducing symptoms in head and neck cancer and colorectal cancer survivors who report a higher burden of tumour-specific symptoms. Oncokompas seems most effective in improving HRQOL in cancer survivors with lower self-efficacy, and in cancer survivors with higher personal control, and higher health literacy.


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 Supplemental data for this article can be accessed [here](#).

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## Introduction

eHealth self-management interventions may have positive effects on health-related quality of life (HRQOL) and symptom burden among cancer survivors, but effect sizes vary considerably [1–4]. It is likely that some cancer survivors may benefit more from eHealth interventions than others, but knowledge of possible moderators is scarce [5–8]. Oncokompas is a web-based self-management application that supports cancer survivors to monitor their HRQOL and cancer-generic and tumour-specific symptoms, and can be used without help from a healthcare professional. Oncokompas provides personalised feedback and information based on scores from patient reported outcome measures (PROMs), and a tailored overview of supportive care options. A tailored care approach is followed i.e.: in case of minor problems information and self-help interventions are proposed, and in case of major problems, professional care is proposed [9,10].

In a previous paper we reported on the efficacy of Oncokompas in a large randomised controlled trial (RCT) among 625 cancer survivors. We showed that Oncokompas had no significant effect on the primary outcome measure patient activation (i.e., knowledge, skills, and confidence for self-management) [11] in the total group, nor in tumour-specific subgroups of head and neck cancer, colorectal cancer, breast cancer, or (non-)Hodgkin lymphoma [12]. However, a significant beneficial effect was found on HRQOL in the total group and several tumour-specific symptoms in survivors of head and neck cancer, colorectal cancer, and non-Hodgkin lymphoma [12]. Effect sizes on HRQOL were small (0.17–0.18) and the effect sizes on symptoms that were significantly different varied from –0.18 to 0.80 up from 1 week to 6 months follow-up [12].

Investigating the effect of potential moderating variables is important to understand the generalizability of research findings in subgroups [13,14]. However, moderating variables of eHealth interventions are not often investigated. In previous RCTs and systematic reviews, several potential moderating factors were explored on the effect of psychosocial interventions among cancer patients. A systematic review showed that cancer patients with lower quality of life, interpersonal relationships and sense of control benefitted more from psychosocial interventions than those who already had adequate resources [8]. An individual patient-data meta-analysis showed that psychosocial interventions significantly improved HRQOL with small effect sizes after treatment, while the intervention effects were larger among younger patients [5].

Intervention effects are mostly in favour of those with a higher education level, higher literacy, and those with higher symptom burden or lower quality of life [5,15,16]. It is expected that in eHealth interventions for cancer survivors clinical factors such as tumour type and stage, type of cancer treatment, and time since treatment, can moderate the effect of the intervention, since symptoms and needs might differ across these subgroups and decrease over time [17,18]. Also,

it could be expected that survivors with a higher need for supportive care benefit more from interventions such as Oncokompas.

The aim of this study was to investigate potential moderating factors, including socio-demographic, clinical, and personal factors, HRQOL, symptoms, and need for supportive care on the efficacy of Oncokompas on HRQOL, symptoms and patient activation. For clinical practice, it is interesting to know which subgroups of cancer survivors are most likely to benefit from an eHealth self-management application such as Oncokompas in terms of HRQOL and symptoms, and patient activation. This knowledge can be used to further tailor eHealth self-management interventions for optimal cancer survivorship care.

## Material and methods

### Study design and population

This study entailed secondary analyses of a randomised controlled trial (RCT) on the efficacy of Oncokompas compared to usual cancer survivorship care. Detailed descriptions of study procedures and primary results can be found elsewhere [12,19]. In short, adult cancer survivors who were treated with curative intent for head and neck cancer, colorectal cancer, or breast cancer, or lymphoma (high- and low-grade non-Hodgkin lymphoma, and Hodgkin lymphoma) 3 months–5 years previously, were asked to participate in the RCT by their (former) treating physician. Exclusion criteria were: no access to the Internet or no email address, severe cognitive impairment, insufficient mastery of the Dutch language, physical inability to complete a questionnaire, and breast cancer survivors with male sex. Survivors were recruited from 14 hospitals in the Netherlands between 12 October 2016 and 24 May 2018. After providing written (online) informed consent and completing the baseline assessment, participants were randomised into the intervention group (direct access to Oncokompas) or control group (access to Oncokompas after a waiting period of 6 months) in a 1:1 allocation ratio, stratified per tumour type. Follow-up assessments were 1-week post-intervention and at 3- and 6-months follow-up. The study protocol was approved by the Medical Ethics Committee of the VU University Medical Centre (2015.523) and the trial was registered in the Netherlands Trial Register (NTR5774).

### Intervention

A detailed description of the intervention has been published previously [12,19]. In short, Oncokompas is an eHealth self-management application that supports cancer survivors to monitor their HRQOL and cancer-generic and tumour-specific symptoms. The main goal is to obtain personalised feedback and information on their scores and a tailored overview of supportive care options. Oncokompas includes various topics in five generic HRQOL domains, which are relevant for

survivors of all tumour types: physical, psychological and social functioning, lifestyle, and existential issues, according to the biopsychosocial model [20]. Besides, various tumour-specific topics are addressed in tumour-specific modules targeting head and neck cancer, colorectal cancer, breast cancer and (non-)Hodgkin lymphoma survivors. Oncokompas consists of three components: 'Measure', 'Learn', and 'Act'. In the 'Measure' component, cancer survivors can complete PROMs on the topic(s) of choice. Data from the 'Measure' component are processed in real-time and linked to feedback in the 'Learn' component. In the 'Learn' component feedback is provided to the cancer survivor by means of a 3-colour system: green (no elevated well-being risks), orange (elevated well-being risks), and red (seriously elevated well-being risks). Cancer survivors receive personalised information on the outcomes, and comprehensive self-care advice. In the 'Act' component, cancer survivors are provided with tailored supportive care options, based on their PROM-scores and expressed preferences (e.g., preference for individual therapy versus group therapy). If a user has elevated well-being risks (orange score), the feedback includes suggestions for self-help interventions. If a user has seriously elevated well-being risks, the feedback includes an advice to contact their medical specialist or general practitioner [12,19,21].

### Outcome measurement

Data on the outcome measures HRQOL, symptoms, and patient activation were collected at time of inclusion (baseline (T0)), 1-week post-intervention (T1), and after 3-months (T2) and 6-months (T3) follow-up.

HRQOL was measured with the EORTC QLQ-C30 summary score (SumSC). The SumSC is based on the five functional scales (physical, cognitive, emotional, social, and role functioning), three symptom scales (fatigue and nausea/vomiting, and pain) and five single items (dyspnoea, insomnia, appetite loss, constipation, diarrhoea) of the QLQ-C30. The SumSC ranges from 0 to 100, with a higher score representing better HRQOL [22].

Tumour-specific symptoms were measured with the EORTC tumour-specific questionnaires. In the present study, those subscales were used on which Oncokompas had a beneficial effect in the RCT [5]: pain in the mouth, social eating, swallowing, coughing and trismus in head and neck cancer survivors (EORTC QLQ-H&N43) [23], weight in colorectal cancer survivors (EORTC QLQ-CR29) [24], and emotional impact in high grade non-Hodgkin lymphoma survivors (EORTC-QLQ-NHL-HG29) [25]. All EORTC scales and single items scores range from 0 to 100 (higher score indicating higher burden of symptoms). Only these subscales were chosen to limit the amount of analyses.

Patient activation was measured with the Patient Activation Measure (PAM), which measures a patients' level of knowledge, skills and confidence for self-management. The PAM score ranges from 0 to 100, with a higher score indicating a higher level of patient activation [11].

### Potential moderators

Potential moderators for the effect on HRQOL and patient activation included socio-demographic, clinical and personal characteristics, and patient activation, mental adjustment to cancer, HRQOL, and need for supportive care, measured at baseline. Potential moderators regarding symptoms included socio-demographic and clinical characteristics, and the baseline score of that symptom.

Socio-demographic characteristics included sex (male, female), age (years), marital status (no partner, partner), education level (low, medium, high), and employment status (employed, not employed), and were measured with a study-specific questionnaire.

Clinical characteristics included tumour type (head and neck cancer, colorectal cancer, breast cancer, or lymphoma), tumour stage (low stage (I or II), high stage (III or IV)), time since diagnosis (categorised into 3–12 months, 12–24 months, and 24–60 months), treatment (none/single treatment, multimodal treatment), and comorbidities (none/one comorbidity, two or more comorbidities). These characteristics were retrieved from the Dutch Cancer Registry, or measured with a study-specific questionnaire [19].

Personal factors included self-efficacy (General Self-Efficacy (GSE) scale [26]), personal control (Pearlin and Schooler Mastery (PSM) scale [27]), health literacy (Functional, Communicative and Critical Health Literacy scale, summary score [28]), health locus of control (Multidimensional Health Locus of Control scale, with internal, powerful others, and chance subscales [29]), and Internet use (<7 h per week, >7 h per week).

Other potential moderators were patient activation (Patient Activation Measure [11]), mental adjustment to cancer (Mental Adjustment to Cancer scale, with summary positive adjustment and summary negative adjustment subscales [30]), HRQOL (EORTC QLQ-C30 summary score [28]), and need for supportive care (Supportive Care Needs Survey 34-items short form, with physical and daily living, psychological, sexuality, and health system, information and patient support subscales, of which scores were dichotomised into no unmet needs and unmet needs [31,32]). Tumour-specific symptoms for head and neck, colorectal and high-grade non-Hodgkin lymphoma were measured with the EORTC tumour-specific questionnaires QLQ-H&N43, QLQ-CR29, and QLQ-NHL-HG29, respectively [24,25,33].

### Statistical analyses

Descriptive statistics were generated for sociodemographic and clinical characteristics. Statistical analyses were performed using the IBM SPSS Statistics version 26 (IBM Corp., Armonk, NY, USA).

To explore moderating factors on the efficacy of Oncokompas compared to care as usual on HRQOL, symptoms and patient activation, from baseline to 6-months follow-up, exploratory linear mixed model (LMM) analyses were performed. The LMM included fixed effects for group (intervention or control), time, their two-way interaction, the



potential moderator, and the two- and three-way interactions with group and time, and a random intercept for subject. A significant three-way interaction effect (group\*time\*moderator) was considered as an indication of a difference in intervention effect on the outcome, between (groups with) different scores on the moderator. A  $p$ -value of  $<.05$  was considered to be statistically significant, and all analyses were conducted according to the intention-to-treat principle.

To interpret the results of a dichotomous moderator variable, post-hoc linear mixed-effect model analyses were performed stratified for each subgroup of the moderator. To interpret the results of a continuous moderator variable, estimated marginal means were calculated for multiple values of the moderator, and data visualisation was performed to interpret the direction of the intervention effect.

## Results

In total, 625 cancer survivors were randomised into the intervention ( $n=320$ ) or control group ( $n=305$ ). Mean age was 63 years (standard deviation (sd) 11), 51% was female, 85% had a partner, and 35% was employed at baseline (Table 1). Furthermore, 30% was diagnosed with head and neck cancer, 24% with colorectal cancer, 24% with (non-)Hodgkin lymphoma, and with 22% breast cancer. The median time since diagnosis was of 27 months (interquartile range (IQR) 16–43). The baseline score of HRQOL (SumSC) was 85.4 (sd

14.3), and the baseline score of patient activation (PAM) was 59.3 (sd 12.5). Socio-demographic and clinical characteristics of participants are summarised in Table 1. Details of the participant flow and dropout have been published previously [12].

Regarding the effect of Oncokompas on HRQOL, self-efficacy moderated this effect (measurement\*group\*self-efficacy,  $F(3,1487)=2.903$ ,  $p=.034$ ) (Table 2). Data visualisation suggested that survivors with low GSE scores (low self-efficacy) benefitted most from Oncokompas, whereas the intervention effect became smaller when GSE scores were higher, and the intervention effect almost disappeared in survivors with high GSE scores (high self-efficacy) (Supplementary Appendix Figure 1).

Personal control also moderated the effect of Oncokompas on HRQOL (measurement\*group\*personal control,  $F(3,1481)=3.478$ ,  $p=.015$ ). Data visualisation suggested that among survivors with low to moderate PSM scores (lower sense of personal control), there was no intervention effect, whereas survivors with high PSM scores (high sense of personal control) benefitted most from Oncokompas, via earlier improvement in HRQOL (Supplementary Appendix Figure 2).

Also, health literacy moderated the effect of Oncokompas on HRQOL (measurement\*group\*health literacy,  $F(3,1478)=2.869$ ,  $p=.035$ ). Data visualisation suggested that there is no intervention effect among survivors with low to

**Table 1.** Baseline characteristics of participants.

|  | Intervention ( $n=320$ ) | Control ( $n=305$ ) |
|--|--------------------------|---------------------|
| Socio-demographic factors                                  |                          |                     |
| Age (mean, sd)   | 63.2 (11.2)              | 63.7 (10.1)         |
| Sex (women) ( $n$ , %)                                     | 158 (49%)                | 158 (52%)           |
| Education level ( $n$ , %) <sup>a</sup>                    |                          |                     |
| Low  | 111 (35%)                | 117 (38%)           |
| Medium   | 105 (33%)                | 85 (28%)            |
| High   | 103 (32%)                | 100 (33%)           |
| Health literacy (mean, sd)                                 | 3.2 (0.5)                | 3.2 (0.5)           |
| Marital status (partner) ( $n$ , %)                        | 265 (83%)                | 269 (88%)           |
| Employment status (employed) ( $n$ , %)                    | 122 (38%)                | 99 (32%)            |
| Clinical factors   |                          |                     |
| Tumour type ( $n$ , %)                                     |                          |                     |
| Breast cancer  | 66 (21%)                 | 72 (24%)            |
| Colorectal cancer  | 80 (25%)                 | 72 (24%)            |
| Head and neck cancer                                       | 99 (31%)                 | 86 (28%)            |
| Lymphoma   | 75 (23%)                 | 75 (25%)            |
| Tumour stage ( $n$ , %)                                    |                          |                     |
| Stage I  | 106 (33%)                | 104 (34%)           |
| Stage II   | 73 (23%)                 | 70 (23%)            |
| Stage III  | 61 (19%)                 | 67 (22%)            |
| Stage IV   | 64 (20%)                 | 52 (17%)            |
| Unknown  | 16 (5%)                  | 12 (4%)             |
| Treatment ( $n$ , %)                                       |                          |                     |
| None/single treatment                                      | 137 (43%)                | 124 (41%)           |
| Multimodal treatment                                       | 183 (57%)                | 181 (59%)           |
| Comorbidities ( $n$ , %)                                   |                          |                     |
| None/one comorbidity                                       | 249 (78%)                | 229 (75%)           |
| Multiple comorbidities                                     | 71 (22%)                 | 76 (25%)            |
| Time since diagnosis (months, median, interquartile range) | 25.0 (16.0–41.0)         | 29.0 (16.5–41.0)    |
| 3–12 months ( $n$ , %)                                     | 39 (12%)                 | 38 (13%)            |
| 12–24 months   | 104 (33%)                | 85 (28%)            |
| 24–60 months   | 177 (55%)                | 182 (60%)           |
| Personal factors   |                          |                     |
| HRQOL (mean, sd)   | 85.3 (14.9)              | 85.4 (13.6)         |
| Patient activation (mean, sd)                              | 59.2 (12.5)              | 59.5 (12.6)         |

<sup>a</sup>Education level was unknown for one participant in the intervention group, and three in the control group.

**Table 2.** Potential moderators of the effect of Oncokompas on patient activation and HRQOL compared to care as usual.

| Potential moderator  | HRQOL                          |                               | Patient activation             |                               |
|--|--------------------------------|-------------------------------|--------------------------------|-------------------------------|
|  | F (3,df) three-way interaction | p value three-way interaction | F (3,df) three-way interaction | p value three-way interaction |
| <b>Socio-demographic factors</b>                                 |                                |                               |                                |                               |
| Sex (men, women)   | 1.214 (1476)                   | .30                           | 0.036 (1414)                   | .99                           |
| Age (years)  | 0.647 (1486)                   | .59                           | 0.442 (1430)                   | .72                           |
| Marital status (no partner, partner)                             | 1.160 (1481)                   | .32                           | 0.591 (1417)                   | .62                           |
| Education level (low, medium, high)                              | 1.699 (1457)                   | .12                           | 1.261 (1399)                   | .27                           |
| Employment status (not employed, employed)                       | 1.468 (1478)                   | .22                           | 0.614 (1418)                   | .61                           |
| <b>Clinical factors</b>  |                                |                               |                                |                               |
| Tumour type (head and neck, colorectal, breast cancer, lymphoma) | 1.780 (1465)                   | .067                          | 0.299 (1402)                   | .98                           |
| Tumour stage (I or II vs. III or IV)                             | 0.961 (1398)                   | .41                           | 1.031 (1340)                   | .38                           |
| Time since diagnosis (3–12, 12–24, 24–60 months)                 | 1.633 (1473)                   | .13                           | 0.262 (1407)                   | .95                           |
| Treatment (0/1, ≥2 treatments)                                   | 0.177 (1474)                   | .91                           | 0.576 (1417)                   | .63                           |
| Comorbidities (0/1, ≥2 comorbidities)                            | 0.960 (1478)                   | .41                           | 0.217 (1410)                   | .88                           |
| <b>Personal factors</b>  |                                |                               |                                |                               |
| Self-efficacy  | 2.903 (1487)                   | <b>.034</b>                   | 0.487 (1435)                   | .69                           |
| Personal control   | 3.478 (1481)                   | <b>.015</b>                   | 1.620 (1431)                   | .18                           |
| Health literacy  | 2.869 (1478)                   | <b>.035</b>                   | 0.847 (1434)                   | .47                           |
| Health locus of control  |                                |                               |                                |                               |
| Internal   | 0.736 (1475)                   | .53                           | 1.085 (1429)                   | .35                           |
| Powerful others  | 1.359 (1476)                   | .25                           | 1.066 (1430)                   | .36                           |
| Chance   | 0.762 (1481)                   | .52                           | 0.107 (1430)                   | .96                           |
| Internet use (<7, >7 h/week)                                     | 1.960 (1470)                   | .12                           | 0.851 (1411)                   | .47                           |
| <b>Patient activation</b>  | 2.124 (1353)                   | .095                          | 0.278 (1460)                   | .84                           |
| <b>Mental adjustment to cancer</b>                               |                                |                               |                                |                               |
| Positive adjustment  | 1.192 (1475)                   | .31                           | 0.498 (1428)                   | .68                           |
| Negative adjustment  | 0.699 (1498)                   | .55                           | 0.540 (1442)                   | .66                           |
| <b>Unmet supportive care needs</b>                               |                                |                               |                                |                               |
| Physical and daily living  | 1.010 (1479)                   | .39                           | 0.756 (1413)                   | .52                           |
| Psychological  | 0.237 (1479)                   | .87                           | 1.259 (1418)                   | .29                           |
| Sexual   | 1.474 (1439)                   | .22                           | 0.376 (1372)                   | .77                           |
| Health system, information and patient support                   | 0.228 (1478)                   | .88                           | 0.416 (1417)                   | .74                           |
| <b>HRQOL</b>   | 0.903 (1617)                   | .44                           | 0.267 (1423)                   | .85                           |

Bold values indicate  $p < .05$ .

moderate health literacy, whereas survivors with high health literacy benefit most from Oncokompas, via earlier improvement in HRQOL (Supplementary Appendix Figure 3).

Regarding the effect of Oncokompas on the investigated symptoms, the baseline score of that tumour-specific symptoms moderated the effect (Table 3). Data visualisation suggested that all survivors with some degree of symptom burden at baseline benefitted from Oncokompas, and the intervention effect became larger when the burden of symptoms was higher (e.g., pain in the mouth in Supplementary Appendix Figure 4). In head and neck cancer survivors, this was the case for pain in the mouth, social eating, swallowing, coughing, and trismus. In colorectal cancer survivors, this was the case for weight. Among non-Hodgkin lymphoma survivors, the baseline score did not moderate the effect of Oncokompas on emotional impacts. Furthermore, among head and neck cancer survivors, Oncokompas was effective to reduce pain in the mouth in women ( $F(3,154)=5.107$ ,  $p=.002$ , but not in men ( $F(3,269)=0.441$ ,  $p=.72$ ).

Oncokompas was effective to improve social eating in HNC survivors without a partner ( $F(3,70)=3.547$ ,  $p=.019$ ), but not in those with a partner ( $F(3,352)=2.055$ ,  $p=.11$ ). Oncokompas was effective to improve trismus in head and neck cancer survivors without a partner ( $F(3,71)=3.613$ ,  $p=.017$ ), but not in those with a partner ( $F(3,354)=0.797$ ,  $p=.50$ ). Age also moderated the effect on trismus. Data visualisation suggested that the intervention effect became larger with increasing age.

Regarding patient activation, none of the investigated factors significantly moderated the effect of Oncokompas (Table 2).

## Discussion

This study aimed to explore which subgroups of cancer survivors may especially benefit from the eHealth self-management application Oncokompas in terms of HRQOL, symptoms, and patient activation. The effect of Oncokompas



**Table 3.** Potential moderators of the effect of Oncokompas on tumour-specific symptoms, compared to care as usual.

| Potential moderator                        | HNC Pain in the mouth<br>(n = 185) |                 | HNC Social eating<br>(n = 185) |                 | HNC Swallowing<br>(n = 185) |             | HNC Coughing<br>(n = 185) |             | HNC Trismus<br>(n = 185) |             | CRC Weight<br>(n = 152) |             | NHL-HG Emotional impact<br>(n = 94) |             |
|--|------------------------------------|-----------------|--------------------------------|-----------------|-----------------------------|-------------|---------------------------|-------------|--------------------------|-------------|-------------------------|-------------|-------------------------------------|-------------|
|  | F (3,df)                           | p value         | F (3,df)                       | p value         | F (3,df)                    | p value     | F (3,df)                  | p value     | F (3,df)                 | p value     | F (3,df)                | p value     | F (3,df)                            | p value     |
| <b>Socio-demographic factors</b>           |                                    |                 |                                |                 |                             |             |                           |             |                          |             |                         |             |                                     |             |
| Sex (men, women)                           | 2.701 (422)                        | <b>.045</b>     | 0.204 (423)                    | .89             | 0.498 (420)                 | .68         | 1.127 (424)               | .34         | 0.817 (425)              | .49         | 1.338 (364)             | .26         | 0.419 (208)                         | .74         |
| Age (in years)                             | 0.800 (424)                        | .49             | 0.684 (424)                    | .56             | 0.231 (421)                 | .88         | 0.215 (427)               | .89         | 3.033 (426)              | <b>.029</b> | 1.897 (364)             | .13         | 0.908 (210)                         | .44         |
| Marital status (no partner, partner)       | 1.930 (426)                        | .12             | 2.952 (423)                    | <b>.032</b>     | 1.260 (422)                 | .29         | 0.255 (427)               | .86         | 3.097 (427)              | <b>.027</b> | 1.046 (358)             | .37         | 0.715 (209)                         | .54         |
| Education level (low, medium, high)        | 0.310 (410)                        | .93             | 0.736 (410)                    | .62             | 0.708 (408)                 | .64         | 1.626 (411)               | .14         | 0.986 (412)              | .43         | 1.105 (356)             | .36         | 0.887 (202)                         | .51         |
| Employment status (not employed, employed) | 0.241 (424)                        | .87             | 0.245 (423)                    | .87             | 0.106 (420)                 | .96         | 0.082 (426)               | .97         | 1.112 (426)              | .34         | 0.810 (362)             | .49         | 0.771 (208)                         | .51         |
| <b>Clinical factors</b>                    |                                    |                 |                                |                 |                             |             |                           |             |                          |             |                         |             |                                     |             |
| Tumour stage (I or II vs. III or IV)       | 1.109 (419)                        | .35             | 0.680 (419)                    | .57             | 0.685 (417)                 | .56         | 1.001 (422)               | .39         | 0.136 (422)              | .94         | 1.476 (358)             | .22         | 0.793 (190)                         | .50         |
| Time since diagnosis                       | 1.043 (423)                        | .40             | 0.438 (419)                    | .85             | 0.398 (417)                 | .88         | 0.956 (425)               | .46         | 0.339 (423)              | .92         | 0.731 (356)             | .63         | 0.811 (201)                         | .56         |
| Treatment (0/1, ≥2 treatments)             | 0.307 (423)                        | .82             | 0.630 (422)                    | .60             | 0.246 (420)                 | .86         | 0.324 (424)               | .81         | 1.305 (425)              | .27         | 1.662 (364)             | .18         | 0.567 (207)                         | .64         |
| Comorbidities (0/1, ≥2 comorbidities)      | 0.689 (425)                        | .56             | 0.470 (423)                    | .70             | 0.707 (421)                 | .55         | 0.611 (429)               | .61         | 0.397 (426)              | .76         | 0.166 (363)             | .92         | 0.346 (208)                         | .79         |
| Baseline score symptom (continuous)        | 5.685 (463)                        | <b>&lt;.001</b> | 8.151 (456)                    | <b>&lt;.001</b> | 2.982 (465)                 | <b>.031</b> | 3.703 (482)               | <b>.012</b> | 4.118 (458)              | <b>.007</b> | 3.303 (396)             | <b>.020</b> | 2.560 (232)                         | <b>.056</b> |

HNC: head and neck cancer; CRC: colorectal cancer; NHL-HG: non-Hodgkin lymphoma, high grade.

Bold values indicate  $p < .05$ .

on HRQOL seems to last longer among cancer survivors with low to moderate self-efficacy, survivors with higher personal control, and those with higher health literacy. In reducing symptoms, Oncokompas was more effective in head and neck and colorectal cancer survivors with higher symptom burden. Among head and neck cancer survivors, Oncokompas was more effective in females (on pain in the mouth), in survivors without a partner (on problems with social eating and trismus), and in older survivors (on trismus). With respect to patient activation, no specific subgroups were found who might benefit more from Oncokompas than others.

Although we aimed to develop a usable web-based application suitable for many cancer survivors, by tailoring information, limiting the amount of text, and making it accessible for low-literate people, health literacy still was found to moderate the effect of HRQOL, in favour of survivors with higher health literacy. Health literacy is known to be an important factor in eHealth interventions [34], and found to be positively associated with HRQOL [16,35,36]. Adaptations are needed to improve the efficacy among those with lower health literacy, for instance by adding multimedia components, such as videos, podcasts, or infographics, or gamification elements [37]. However, it might be that despite these adaptations this group might benefit more from other types of interventions, e.g., face-to-face or group interventions.

Interestingly, Oncokompas seems more effective in cancer survivors with low to moderate self-efficacy. Self-efficacy is a concept that influences how people think, feel, motivate themselves, and act [38]. Our finding suggests that a low-intensive intervention such as Oncokompas provides help or tools to people with lower motivation or lower self-esteem to act. Moderating effects of self-efficacy were also found with an intervention on treatment information in breast cancer support groups; however, the effect on the outcome emotional well-being was in favour of women with higher self-efficacy [39]. On the other hand, the intervention effect of a psychoeducational intervention for men with prostate cancer has been shown in another study to be in favour of those with lower levels of prostate-specific self-efficacy [40].

Furthermore, the intervention effect was also in favour of those with high personal control. Personal control, or mastery, refers to the degree to which controlling factors that influence life situations can be perceived, and it has been found important for HRQOL and well-being [27,41]. The improvements in HRQOL that were found in this group, suggest that fully-automated self-management interventions, can provide support to those with high feelings of mastery, to enhance their sense of mastery over their HRQOL and symptoms.

The intervention effect in favour of those with lower self-efficacy and higher personal control seems to be contrary. Examining the study population in the current study, persons with lower self-efficacy were not the same persons as those with higher personal control. It could be that cancer survivors with lower self-efficacy need a push to take action, and with Oncokompas, they have the tools to improve HRQOL. The effect among cancer survivors with higher personal control might be because they feel in control with Oncokompas,

which leads to an earlier improvement in HRQOL. However, because the interaction effects were small, it could be that these findings were found by chance. Moderating effects of mastery and self-efficacy on the effects of eHealth interventions are not often investigated among cancer survivors. Further research is needed to confirm whether the identified moderating factors are moderating factors of eHealth interventions in general, or whether these factors especially moderate the effect of fully-automated self-management interventions.

Remarkably, baseline HRQOL did not moderate the effect on HRQOL, but baseline symptoms did moderate the effect on symptoms. This suggests that improvement of HRQOL is possible for every cancer survivor, regardless of having a low or high HRQOL at the start of the intervention, and the benefit of Oncokompas might be through reducing symptom burden. Evidence on moderating effects of baseline values of HRQOL is inconsistent [5,42].

As we demonstrated previously, Oncokompas was not effective in improving patient activation [12]. The current analyses showed there are also no subgroups for which patient activation was improved, so it might be that there is truly no effect of Oncokompas on survivors' skills, knowledge and confidence for self-management. This may be explained by the fact that the study population comprises cancer survivors who had access to the Internet, and who were doing relatively well in terms of HRQOL, patient-physician interaction, adjustment to cancer, and unmet supportive care needs. Another explanation may be that most were long-term survivors (>2 years after diagnosis), who might already found the information and support they need to build their skills and confidence to manage cancer-related concerns [12,17]. Since the main aim of Oncokompas is to improve HRQOL and reduce symptom burden, we do not think that the content of Oncokompas should be adapted towards an improvement of patient activation. However, further research is needed to understand how cancer survivors use Oncokompas, which topics are chosen, and how usage and engagement can be improved. Further research is also needed to confirm the moderating effects that were found, and to enhance the understanding of how and under what circumstances eHealth interventions lead to beneficial effects.

The strengths of this study are the large sample size, with participants from 14 hospitals across the Netherlands, and that it includes various categories of moderators. However, the results of this study should be considered with caution, because of some limitations. This study was not powered to detect differences in secondary outcomes, and to perform secondary exploratory analyses to detect moderating factors. Therefore, it is possible that important moderating factors were not identified, because of a lack of power. Also, with many potential moderators, and multiple outcome measures, many separate models were analysed in the total group. As a result, the observed effects might have been found by chance. Because the analyses were only exploratory, and there is no consensus on how to apply corrections for multiple testing [43], no corrections for multiple testing have been made. In our previous publication, no effects were found on other investigated secondary outcomes, such as

self-efficacy and supportive care needs. It could be that these outcomes are improved in specific subgroups of cancer survivors, but we decided to limit the number of analyses by focussing on HRQOL and symptoms, and the primary outcome patient activation in this study.

This study provides valuable information on improving the efficacy of future eHealth self-management interventions targeting cancer survivors. Cancer survivors with low to moderate self-efficacy, those with higher personal control, and those with higher health literacy showed larger HRQOL benefits of Oncokompas. Furthermore, Oncokompas is especially effective to improve tumour-specific symptoms among survivors of head and neck cancer and colorectal cancer with higher symptom burden. Targeting these subgroups of survivors might lead to improvements in the intervention effect of eHealth self-management interventions.

## Ethical approval

All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

## Disclosure statement

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